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PREVALENCE OF PLASMODIUM SPECIES AND ASSOCIATED DEMOGRAPHIC AND RISK FACTORS IN CANCER, SICKLE CELL AND FEBRILE PATIENTS ATTENDING A TERTIARY HOSPITALS IN ZARIA-NIGERIA

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PREVALENCE OF PLASMODIUM SPECIES AND ASSOCIATED DEMOGRAPHIC AND RISK FACTORS IN CANCER, SICKLE CELL AND FEBRILE PATIENTS ATTENDING A TERTIARY HOSPITALS IN ZARIA-NIGERIA

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ABSTRACT

Background: **The duo plasmodium falciparum malaria infection and sickle cell disease prevalence are established, and consequent morbidity and mortality are significant in parts of Nigeria. The emerging increase of cancer morbidity and mortality impact is expected to complicate these conditions. It is against this not so clear relationship that this study is set.**

Objective: **To determine plasmodium prevalence and associated demographic and risk factors in cancer, sickle cell and febrile patients.**

Methodology: **A comparative cross-sectional prevalence in which participants were randomly recruited from a tertiary hospital in Kaduna State Nigeria. A total of 279 cancer and sickle cell and febrile patients were assessed for the plasmodium infection and parasitaemia by the Giemsa stain methods.**

Results: **The plasmodium prevalence was 63.4%. The cancer, sickle-cell and febrile patients had prevalence of 89.5%, 76.9% and 48.2% with parasitaemia observed in 39.5%, 7.7% and 16.5% respectively. The prevalence was higher in females (67.5%) than males (58.4%) and high parasitaemia in 20.8% of females and 14.4% of males. Prevalence was over 50% within age groups 11 – 20 and 51 – 70 years. Kaduna residence had lower prevalence (58.0%) than those from outside Kaduna (72.8%). The single, divorced, widow(er), farmers and those with no formal occupation had a prevalence of over 50%. Participants with primary education had the highest prevalence (87.5%). Prevalence was over 80% for head and neck, lung, breast and cervical cancer**

Conclusion: **The high prevalence of plasmodium infection in cancer and sickle cell patients necessitates monitoring for plasmodium infection and prompt interventions.**

INTRODUCTION

Malaria has remained endemic in the sub-Saharan Africa with a high mortality[1]. Despite recent reductions in the overall malaria case incidence, malaria remains a leading cause of morbidity and mortality in the developing world[1]. In 2012, there were an estimated 207 million cases of malaria and over 600,000 deaths[1]. The majority of malaria deaths (90%) occur in children in Africa, where falciparum malaria accounts for as many as one in six childhood deaths and is the biggest killer of African children between the ages of 1 and 4 years[2]. Malaria affects 3.3 billion people, or half of the world's population. WHO estimates 216 million cases of malaria occurred in 2010, with 81% in the African region. WHO also estimates there were 655,000 malaria deaths in 2010, with 91% in the African Region, and 86% were children under 5 years of age[3]. Malaria is the 3rd leading cause of death for children under five years worldwide, after pneumonia and diarrheal disease[3].

Cancer continues to ravage the world being considered as a major public health problem just like malaria[4]. A study in 2014 reported over 13 million new cancer with record cancer deaths of about 70% and associated the deaths to countries within the low- and middle-income earners[5].

Cancer mortality is on the increase and some studies has defined an association between plasmodium infections and leading to either suppression or induction of cancer[6,7]. Infections with plasmodium is known to induce immune suppression and depletion of the red blood cells and increased susceptibility to other infectious agent such as viruses some of which could induce cancer[8]. Individuals infected with the malaria parasite were prone to infections by Salmonella, herpes zoster virus, hepatitis B virus, Epstein Barr virus reactivation or infections with Moloney murine leukemia virus[9]. The infection with strains of plasmodium may eventually lead to cure of cancer as infections with plasmodium leads to the production of certain proteins that may inhibit cancer progression[9]. Certain viruses such as Epstein Barr virus acquires its tumourigenecity by utilizing certain proteins produced during malaria infection as co-factor[10]. Individuals with the sickle cell trait associated with the homologues gene for haemoglobin SS (HbSS) exhibit resistance to plasmodium infection[11]. In spite of this, in Africa, 80% of individuals born with the sickle cell traits die annually of malaria related illness[12]. This has increased the recommendation of antimalarial chemoprophylaxis for these patients[13].

This present study was aimed at determining the prevalence of plasmodium in cancer, febrile and sickle cell patients attending a selected tertiary hospital in Zaria

METHODOLOGY

Study Area: The study was carried out in Ahmadu Bello University Teaching Hospital, Shika, Zaria, Kaduna State, Nigeria. Kaduna State is in the Northern Nigeria and is about 1000km from the Atlantic Ocean. It is located on a latitude of 11°12'N and a longitude of 07°37'E with a population of 6,113,503[14]. The hospital being the largest Teaching hospital in

the northern Nigeria and serves the health need in general and specialized clinical medicine and as referral centre for other health centres and hospitals in the state and other neighboring state.

Study Population: The participants were patients who reported to ABUTH, Zaria presenting with fever (febrile group), Cancer and sickle cell groups. The patients were selected irrespective of their gender and age.

Study entry: Included were patients presenting with febrile illness, cancer irrespective of the type and sickle cell anaemia. Signing of informed consent was mandatory for study entry. Patients with no proof of diagnosis were excluded.

Study Design: The study was comparative cross sectional.

Ethical considerations: Ethical approval was obtained from the Ethical Committee of the ABUTH Shika-Zaria (ABUTHZ/HREC/Q7/2015). All patients who required attention were served appropriately. All patient were handled purely for study and confidentiality maintained for all cases in the study.

Sample Size Calculation: The sample size was calculated using the formula below using the prevalence of 23.8% obtained in a previous in Kano, Nigeria[15].

$$N = \frac{PQ}{(E/Z)^2}$$

$$n = 23.8 \times 76.2 / (5/1.96)^2 = 279.0$$

The sample size calculated was 279 hence, 279 samples were collected and used for the study.

Procedure of enrollments of patient: Patient enrolment was based on a ratio of 4:2:1 for febrile patients, cancer and sickle cell patients based on the patient turn out to the hospitals. Thus, the samples were 164, 76 and 39 for the febrile cancer and sickle patients respectively giving a total of 279.

Febrile Patients: Patients reporting to the hospital that had fever of known cause yet to be diagnosed. Fever is considered when the body temperature was above 37.5˚C.

Cancer Patients: Patients diagnosed with cancer irrespective of type and site by the physicians were randomly selected from the oncology clinic and included in the study

Sickle Cell Patients: Patients with the HB SS genotype were randomly recruited from the sickle cell clinic

Sample Collection, Analysis and Data Management: Venous blood one milliliter was obtained into ethylene diamine tetra acetic acid (EDTA) tube by the hospital laboratory staff at the general laboratory of ABUTH, Shika-Zaria. The blood was immediately used for thick and thin blood smears preparation on clean, grease-free slides for malaria parasite detection by light microscopy. The blood samples were analysed for presence of *Plasmodium* species and their density density/μL of blood.

Microscopy for detection of Plasmodium species and parasite density/μL determination: Thin and thick blood smears were carried prepared for each of the samples obtained to determine presence of Plasmodium species and their density/μL of blood of the selected patients according to the methods as previously described[18]. Both the thick and thin smears were stained with Giemsa stain then observed for *Plasmodium* species and the finding documented.

The parasite density was estimated by multiplying the average number of parasites observed per high power field (100x objective and 10x eyepiece) by 500. Between10-50 fields were examined, depending on parasitaemia, to determine the average number of trophozoites per high power field (HPF)[16].

Data Management: Proforma structured questionnaires were used to collect information on patient's sociodemographic data, clinical data and some risk factors that might be associated with Plasmodium infection among participants. The data was analyzed using SPSS version 17.0 statistical software. ANOVA, Odd ratio and Chi-square (χ^2) were also used to test the association between variables. Level of significance (P) and confidence interval (CI) were at P<0.05.

RESULTS

An overall malaria prevalence was 63.4% with the most prevalent being *Plasmodium falciparum* (100%) (Table 1). The cancer group had the highest prevalence (89.5%) followed by the sickle-cell group (76.9%) and the least being the febrile group (48.2%) (P<0.05) (Table 1). It was also observed that 39.5% of the cancer patients, 16.5% of the febrile patients and 7.7% of the sickle-cell group had high parasitaemia (P<0.05) (Table 1).

Table 1

The Incidence and Density of P. falciparum among the febrile, Cancer and Sickle Cell Patients Selected Patients Attending ABUTH, Zaria

Study Group	Number Examined	Number Positive (%)	Parasite Density (%)			P value
			Low	Moderate	High	
Febrile group	164	79 (48.2)	35 (21.3)	17 (10.4)	27 (16.5)	P = 0.002 df – 2 χ^2 = 49.10
Cancer group	76	68 (89.5)	18 (23.7)	20 (26.3)	30 (39.5)	
Sickle-cell group	39	30 (76.9)	21 (53.9)	6 (15.4)	3 (7.7)	
Total	279	177 (63.4)	74 (26.5)	43 (15.4)	60 (21.5)	

Key: *Low: 3,500-10,000 parasites/µL of blood. Moderate: 11,000-20,000 parasites/µL of blood. High: ≥ 25,000 parasites/µL of blood.*

The *P. falciparum* prevalence and parasitaemia was higher in females (67.5%; 20.8%) than males (58.4%; 14.4%) (Table 2).

Table 2

The Incidence and Density of P. falciparum in Relation to Sex of the Selected Patients Attending ABUTH, Zaria Kaduna State

Sex	Number Examined	Number Positive (%)	Parasite Density		
			Low (%)	Moderate (%)	High (%)
Male	125	73 (58.4)	29 (23.2)	16 (12.8)	18 (14.4)
Female	154	104 (67.5)	45 (29.2)	27 (17.5)	32 (20.8)
Total	279	177 (63.4)	74 (26.5)	43 (15.4)	60 (21.5)

Key: *Low: 3,500-10,000 parasites/µL of blood; Moderate: 11,000-20,000 parasites/µL of blood; High: ≥ 25,000 parasites/µL of blood.*

All the age group had a prevalence of over 50%. However, age groups 61 – 70, 51 – 60 and 11 – 20 had high prevalence of 100%, 75.6% and 75% respectively (p = 0.011) (Table 3).

Table 3

The Incidence and Density of P. falciparum in relation to the age group of studied patients

Age-group	Number Examined (%)	Number of Positive (%)		Overall Positive cases (%)	P value
		Males	Females		
0-10	34 (12.2)	11 (32.4)	12 (35.3)	23 (67.6)	P = 0.011 (df – 6)
11-20	44 (15.8)	14 (31.9)	19 (43.2)	33 (75.0)	
21-30	53 (19.0)	13 (24.5)	15 (28.3)	28 (52.8)	
31-40	59 (21.2)	15 (25.4)	19 (32.2)	34 (57.6)	
41-50	44 (15.8)	6 (13.6)	18 (40.9)	24 (54.6)	
51-60	41 (14.7)	11 (26.8)	20 (48.8)	31 (75.6)	
61-70	4 (1.4)	3 (75.0)	1 (25.0)	4 (100.0)	
Total	279 (100.0)	73 (26.2)	104 (37.3)	177 (63.4)	

However, those from Kaduna had higher malaria cases (58.0%) than their counterparts from outside Kaduna state (72.8%). The difference in sex among Kaduna resident was not significant while the association among those from the neighborhood states was statistically significant (P<0.05) (Table 4).

Table 4

Place of residence and distribution of P. falciparum

Place of Residence	Sex	Number Examined (%)	Number Positive (%)	P value
Kaduna State	Male	82 (46.6)	47 (57.3)	P = 0.181 df - 1
	Female	94 (53.4)	55 (58.5)	
	Total	176 (100.0)	102(58.0)	
Outside Kaduna State	Male	43 (41.8)	26 (60.5)	P = 0.05 df - 1
	Female	60 (58.2)	49(81.7)	
	Total	103 (100.0)	75(72.8)	

The single, divorced and widow(er) had prevalence of 75.5%, 83.3% and 75% respectively (Table 5). All patients irrespective of the type of occupation had a prevalence of 50% and above with the exception of the artisans that had 44.8%. The farmers and those with no formal occupation had higher prevalence of 73.3 and 73% respectively (p = 0.017). Participants with tertiary education had a prevalence of 41.2%, while those with primary education having the highest (87.5%) and this was statistically highly significant (p = 0.002) (Table 5).

Table 5

Selected sociodemographic factors and P. falciparum distribution

	Number Examined	Number Positive (%)	P Value
Marital Status			χ^2 = 46.09; df=3; p=0.067
Single	102	77(75.5)	
Married	163	89(54.6)	
Divorced	6	5(83.3)	
Widow(er)	8 (2.9)	6(75.0)	
Total	279 (100.0)	177 (63.4)	
Occupation			χ^2 = 67.08; df=5; P=0.017
Civil Service	54	27(50.0)	
Artisan	29	13(44.8)	
Business	32	19(59.4)	
Farming	15	11(73.3)	
Pensioner	12	7(58.3)	
No formal Occupation	137	100(73.0)	
Total	279	177(63.4)	
Educational Level			χ^2 = 21.71; df=3; p=0.002
No formal Education	58	38(65.5)	
Primary	64	56(87.5)	
Secondary	63	44(69.8)	
Tertiary	94	39(41.2)	
Total	279	177(63.4)	

Malaria parasitaemia for head and neck cancers and Lung cancer were 100.0% followed by the breast cancer 90.5%, was cervical cancer 81.82% This was statistically significant p=0.0486 (Table 6).

Table 6

The distribution of P. falciparum in respect of the type of Cancer

Cancer Type	Number Examined	Number Positive (%)	P Value
Prostate	2	1(50.0)	χ^2 = 19.01; df=6; p=0.0486
Breast	21	19(90.5)	
Intestinal	6	5(83.3)	
Lung	4	4(100.0)	
Head and Neck	18	18(100.0)	
Skin	14	12(87.7)	
Cervical	11	9(81.8)	
Total	76		

DISCUSSION

In this study, only a single species of Plasmodium: *Plasmodium falciparum* was found among the study population. This finding suggests that *Plasmodium falciparum* is the most prevalent species the study area. This is consistent with the study by Udomah *et al*,[17] performed within similar climatic condition in Sokoto State which also indicated that

Plasmodium falciparum was responsible for all the cases of malaria parasitaemia found among their study subjects and Abah and Temple[18] report's report in Bayelsa State. *P. falciparum* remains the most prevalent malaria parasite on the African continent. It is responsible for most malaria-related deaths globally[19].

In this study, the prevalence of *P. falciparum* malaria was 63.4%. This prevalence is lower than the 80.5% reported by Olasehinde *et al*.[19] in Ota-Nigeria and the 90.4% malaria prevalence reported in Abia State-Nigeria by Kalu, *et al*.[20]. In Sokoto, Nigeria, Udomah *et al*.[17] reported a prevalence of 52.2%. These findings show the magnitude of the malaria burden prevalent in Nigeria in which *P. falciparum* infection occurs throughout the year[21]. In southern Nigeria, Abah and Temple[18] reported a malaria prevalence of 63.3% among their Bayelsa state study population, similar to the prevalence obtained in this study. This finding is contradicted by that of Adedoja, *et al*.[22], who found higher malaria prevalence among males than in females, among their study population in Ekiti State-Nigeria. However, Kalu *et al*.[20] found higher infection prevalence among females than males in Abia state-Nigeria, corroborating the findings in this study. Since malaria is not a sex-linked disease, differences in exposure to the malaria vector among the two sexes, as well as differences in immunity to parasitic infections explains the finding in this study in which more of the females were infected with *falciparum* malaria than their male counterparts. Malaria remains highly endemic throughout Nigeria[23]. W.H.O. estimated that there were 214 million cases of malaria and 438, 000 deaths. Sub-Saharan Africa bears a disproportionately high share of the global malaria burden. The region was home to 88% of malaria cases and 90% of malaria deaths[1]. Furthermore, the tropical climate as well as population density with the attendant poverty increases the exposure and proliferation of the parasite and increase in infection.

Furthermore, high prevalence was observed across all ages though the aged (31 – 70yrs) had highest. The high prevalence found among the 61-70 age-group reflects waning immunity typical of the aging process. Also, the elderly often remain indoors especially at night which is the pick biting period for the vector. This finding differs from that of Kalu *et al*.[20] who reported higher malaria infection among the 21-30 age-group of their study population. The participants that had no formal education and artisans had higher prevalence. This might not be unconnected to the level of education and poverty leading to inability to afford protective and mosquito control facilities.

There was a significant statistical association between the type of cancer and infection with *P. falciparum* among the selected patients attending ABUTH, Zaria. A higher malaria parasite density was found among participants with head and neck and breast cancers, while the least parasitaemia was found among participants with prostate cancer. Epstein-Barr virus latent infection has been linked to several malignant cancers that occur in the head and neck regions as the oropharyngeal epithelium is the main site of the virus proliferation after infection[24]. This further corroborates the findings in this study about the relationship between EBV and malaria, since participants with EBV-related cancers had higher malaria parasitaemia than participant with other cancer types not known to be linked to EBV.

The result demonstrated some level of protection in those having the sickle-cell trait and agrees with reported by Mulama *et al*.[25] in Kenya. It has been suggested that the sickle haemoglobin gets in the way of the *Plasmodium* parasite infecting red blood cells, thus reducing the number of parasites that actually

infect the host and hence confer some protection against the disease[26]. Similarly, in Oyo-Nigeria, Akhigbe *et al*.[27] reported that dominant homozygotes (HbAA) were more susceptible to plasmodium parasite infection than the sickle heterozygotes (HbAS), while the recessive homozygotes (HbSS) were most vulnerable to malaria than the other two members of the group the mechanism underlying this protective effect thus remained elusive[28].

CONCLUSION

The study thus established that Plasmodium remains prevalent in the study area. The cancer, sickle-cell and febrile patients had prevalence of 89.5%, 76.9% and 48.2%. The prevalence was significant with a high parasite density of 16.5%. 39.5% and 7.7% among febrile, cancer and sickle cell patients respectively. A higher parasitaemia was found among 32 females with a parasite density of 20.8% while 18 males had a high parasite density of 14.4%, while all the age group had a prevalence of over 50%. Malaria parasitaemia was highest in head and neck cancers and Lung cancer patients, followed by the breast and cervical cancer patients. It is recommended that Cancer and Sickle cell patients should be monitored for plasmodium infection.

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